REMARKS

Status of the Claims

Claims 1-39 are pending and claims 19-31 are under consideration in this application, claims 1-18 and 32-39 having been withdrawn for allegedly being drawn to separate inventions.

Claims 19 and 25 are amended to specify that the B7-H1 molecule for which the relevant antibodies are specific is human B7-H1 and that the levels of human B7-H1-specific antibodies are tested for. In addition, claim 25 is amended to specify that an elevated level of the antibodies correlates with an active stage of the relevant disease or pathological condition. These amendments are supported by the specification, e.g., at page 1, lines 13-14; page 12, lines 24-28; pages 14-16; and page 41, line 27, to page 42, line17.

No new matter is added by any of the amendments made herein.

After entry of this Amendment and Response, claims 1-39 will be pending and claims 19-31 will be under consideration in this application.

Title of the Application

The Examiner states that the present title is not descriptive (page 3, lines 5-6, of the Office Action). While not agreeing with this position, in order to expedite prosecution of the application, Applicants have replaced the title with one that is more descriptive of the invention as embodied by the present claims.

Trademarks

In response to the comments on page 3, lines 8-13, of the Office Action, Applicants have capitalized each letter of trademarks in the application. Applicants submit that at each occurrence of a trademark, the relevant text contains a generic description of the relevant trademarked item. Moreover, Applicants have added the symbols "™" and "®", as appropriate.

Claim Objection

Applicants thank the Examiner for pointing out the typographic omission in claim 19, which has been corrected.

35 U.S.C. § 112, second paragraph, rejections

Claims 19-31 stand rejected as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicants regard as the invention.

From the comments on page 4, lines 7-13, of the Office Action, Applicants understand the Examiner's position to be that one skilled in the art would not know which of various methods known in the art for "identifying a subject that is suspected of having, or is likely to develop a disease or pathological condition with symptoms that are caused directly, or indirectly, by activated T cells" would be covered by the instant claims. Applicants respectfully submit that the claim is not limited to any single method or range of methods for performing the relevant identification. Any method resulting in such identification is included in the scope of the claims. On page 12, lines 8-23, of the instant specification are listed various diseases and conditions that are mediated, directly or indirectly, by activated T cells. These include autoimmune diseases, allergies, delayed type hypersensitivity, and allograft and xenograft rejection responses.

Applicants respectfully submit that those ordinarily skilled in the art (e.g., clinicians that treat such diseases and conditions) would be very familiar with the signs and symptoms exhibited by subjects "suspected of" having the diseases and/or conditions. Thus, for example, the American College of Rheumatology has promulgated criteria for diagnosing rheumatoid arthritis (RA) (see, e.g., page 37, lines 30-31, of the instant specification). Moreover, they would similarly be familiar with methods of identifying subjects that are "likely to develop" such diseases and conditions. For example, subjects with a family history of autoimmune disease or certain allergies or those living and/or working in geographic locations or physical environments that are associated with an increased incidence of certain autoimmune diseases or allergies would be considered "likely to develop" such diseases or conditions. In addition, subjects that have undergone allogeneic or xenogeneic transplantation procedures would also be considered "likely to develop" graft rejection responses.

From the comments on page 4, lines 14-19, of the Office Action, Applicants understand the Examiner's position to be that one of ordinary skill in the art would not know what constitutes "an elevated level of one or more B7-H1-specific antibodies" as the phrase is used in the instant claims. Applicants disagree with this position and respectfully submit that such artisans (e.g., clinicians or scientists) would understand the term "elevated" to mean "above normal". They would also know that, in the art, a "normal level" of some factor is generally the level of the factor in subjects without the relevant disease or condition. They would also know simple methods of establishing the mean level of the antibody in such "normal" subjects. Any subject having a level of antibodies significantly different from such a mean level would be a subject with an "elevated" level of the antibodies.

From the comments on page 4, lines 20-25, of the Office Action, Applicants understand the Examiner's position to be that one ordinarily skilled in the art would not know what "level of antibody" correlates with what "stage of disease or pathological condition" or the amount or degree of such correlation. Applicants respectfully disagree with this position. Those ordinarily skilled in the art (e.g., clinicians and scientists) would know very well that such correlations are made by comparing the level of antibody in a subject with the levels of antibody in "standard" subjects having different defined stages of the disease or condition and would know how to perform studies to ascertain such "standard" levels. The level or amount of correlation will likely vary greatly from one disease or condition to another but will be readily ascertainable from the entirely routine studies mentioned above designed to obtain "standard" levels.

In light of the above considerations, Applicants respectfully request that the rejections under 35 U.S.C. § 112, second paragraph, be withdrawn.

35 U.S.C. § 112, first paragraph, rejections

(a) Claims 19-31 stand rejected as allegedly containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

From the comments on page 5, line 8, to page 6, line 21, the Office Action, Applicants understand the Examiner's position to be that the instant specification does not provide:

(a) a sufficient definition of B7-H1; and

(b) structural or functional descriptions of B7-H1 and, thus, that the Applicants are not in possession of antibodies to generically recited "B7-H1".

As noted above, Applicants have amended claims 19 and 25 to specify that the B7-H1 molecule specified by the claims is human B7-H1. Moreover, a scientific article (Dong et al. (1999) Nature Med. 5:1365-1369; copy enclosed as Exhibit A) published before the priority date of the instant application and cited several times in the application (e.g., at page 11, line 16; page 38, lines 24-25; and page 39, line 11) provided the amino acid sequence of human B7-H1 and described polyclonal antibodies specific for B7-H1. Other references describing B7-H1-specific monoclonal antibodies will be provided if the Examiner so wishes. In light of these considerations, Applicants respectfully submit that they were in possession of the claimed invention at the priority date of instant application.

Applicants contend that, given the state of the art as of the priority date of the instant application, one of skill in the art would know and understand that the term "human B7-H1" refers to a known human protein. Moreover, Applicants submit that the sequence and biological properties of human B7-H1 were well known and widely available based on the publicly accessible literature. Accordingly, one ordinarily skilled in the art would understand that "human B7-H1" would identify a known human protein with defined metes and bounds.

In *Falko-Gunter Falkner v Inglis* (448 F.3d 1357, 2006 WL 1453040, Fed.Cir. May 26, 2006), the Federal Circuit held that "[T]here is no per se rule that an adequate written description of an invention that involves a biological macromolecule must contain a recitation of known structure." (*Falko-Gunter Falkner*, 448 F.3d 1357, 2006 WL 1453040, *14; Exhibit 3). There, the court held that "where, as in this case, accessible literature sources clearly provided, as of the relevant date, genes and their nucleotide sequences (here 'essential genes'), satisfaction of the written description requirement *does not require* either the recitation or incorporation by

reference (where permitted) of such genes and sequences." *Falko-Gunter Falkner*, 448 F.3d 1357, 2006 WL 1453040, *17 (emphasis added).

As the part of 35 U.S.C. § 112 at issue in *Falko-Gunter Falkner* was also § 112, first paragraph, Applicants submit that the analysis applies to the issue raised by the Examiner in the instant application. Moreover, if the published literature is readily available, as it is here, and one of skill in the art would understand it to refer to a particular protein, Applicants submit that, by satisfying the first paragraph of § 112, the second paragraph, is also satisfied. "Human B7-H1" was well known in the art as of the priority date of the instant application, as were "antibodies specific for human B7-H1", and the terms were used and understood by one of skill in the art to each refer to a specific protein and antibodies specific for that specific protein. Applicants submit that, in view thereof, they were in sufficient possession of generically recited antibodies to B7-H1 to satisfy the requirements under § 112, first paragraph (and, incidentally, second paragraph). Accordingly, Applicants respectfully request that the rejection of claims 19-31 under 35 U.S.C. § 112, first paragraph be withdrawn.

(b) Claims 19-31 stand rejected as allegedly containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention.

(i) Rejection in section 13 of the Office Action

From the comments on page 7, line 1, to page 8, line 11, of the Office Action, Applicants understand the Examiner's position to be that the specification does not enable the claimed methods of diagnosis of RA and monitoring the progress of RA. Applicants respectfully disagree with this position.

First, with respect to the comment on page 7, lines 23-26, of the Office Action, Applicants submit that, even under the broadest interpretation of the phrase, "subjects that are suspected of having, or are likely to develop, a disease" could not be construed to include the entire population. Thus, those "suspected of having the disease" would by definition have to

have, at a minimum, a symptom or range of symptoms established by those skilled in the art to be at least suggestive of the relevant disease. Moreover, those skilled in the art, would expect that subjects "likely to develop the disease" would be subjects having, at a minimum, risk factors for that disease (see comments above in the response to the rejection under 35 U.S.C. § 112, second paragraph). Thus, the pool of subjects to whom the claimed methods of the invention would be only a small fraction of the entire population. These considerations, and the fact that 29% of subjects having RA (as established by other criteria) had antibodies specific for human B7-H1 while only 4 % of normal subjects had such antibodies, indicate that the method of claim 1 is useful for the diagnosis of RA.

Moreover, in this regard, Applicants respectfully submit that there is no requirement for patentability that any given method or process function at 100% efficiency or better than prior art methods. The only requirement is that the claimed methods function as claimed and defined by the specification (see, for example, *Raytheon Co. v. Roper Corp. 724 F.2d 951, 958, 220 USPQ 592, 598 (Fed. Cir. 1983), cert. denied, 469 U.S. 835 (1984).* "An invention need not be the best or the only way to accomplish a certain result, and it need only be useful to some extent and in certain applications...[;]" *Cf. Custom Accessories, Inc. v. Jeffrey-Allan Industries, Inc., 807 F.2d 955, 960 n.12, 1 USPQ2d 1196, 1199 n.12 (Fed. Cir. 1986`).* "It is possible for an invention to be less effective than existing devices but nevertheless meet the statutory criteria for patentability[;]" or *E.I. du Pont De Nemours and Co. v. Berkley and Co., 620 F.2d 1247, 1260 n.17, 205 USPQ 1, 10 n.17 (8th Cir. 1980).* "The claimed invention must only be capable of performing some beneficial function... An invention does not lack utility merely because the particular embodiment disclosed in the patent lacks perfection or performs crudely....."). Indeed, as in the diagnosis of many, if not all, clinical conditions, more than one methodology is generally used to test for the presence of the clinical condition.

With respect to the comments on page 8, lines 1-7, of the Office Action, Applicants emphasize that all patients compared in the study referred to were already diagnosed as having RA. The investigators determined the fractions of B7-H1 antibody-positive and B7-H1-negative RA patients having active RA. Applicants respectfully submit that, given that all the patients

had already been determined to have RA, the difference in the presence of active RA in the two groups is not very small (33%) and indicates, as recited in the instant specification (e.g., in Example 3) and in the Dong et al. reference (J. Clin. Investigat. (2003) 111:363-370) cited by the Examiner (e.g., Abstract; paragraph spanning page 366, column 2, and page 367; page 369, first two sentences of paragraph spanning columns 1 and 2; and page 369, column 2, paragraph 2, first sentence), that presence of B7-H1-specific antibodies in RA patients is correlated with RA progression, thereby providing strong support for the method of claim 25

In this regard and with respect to the comments on page 8, lines 3-7, of the Office Action, Applicants respectfully point out that the Dong et al. reference cited by the Examiner does not state "that it is unknown whether or not B7-H1 autoantibodies are correlated with active disease, due to the semiquantitative nature of the ELISA assay used in these studies, and subjective diagnostic standards for active disease." Indeed, the reference states quite the opposite, i.e., that the presence of B7-H1-specific autoantibodies is correlated with active disease (e.g., Abstract; paragraph spanning page 366, column 2, and page 367; page 369, first two sentences of paragraph spanning columns 1 and 2; and page 369, column 2, paragraph 2, first sentence). It is in regard to a possible quantitative correlation between the level of autoantibody and active disease that the Dong et al. reference cited by the Examiner is uncertain (page 369, column 2, paragraph 2, second sentence).

In light of the above considerations, Applicants respectfully submit that it would not involve excessive experimentation to practice the claimed methods as they relate to diagnosis and monitoring of the progression of RA and therefore request that the rejection be withdrawn.

(ii) Rejection in paragraph 14 of the Office Action

From the comments on page 8, line 12, to page 9, line 10, of the Office Action, Applicants understand the Examiner's position to be that the instant specification does not provide sufficient enablement for the claimed methods as they relate to diseases or pathological conditions in general caused by activation of T cells and to autoimmune diseases. Applicants respectfully disagree with this position.

For the reasons given above, Applicants submit that the claims now under consideration, as they relate to RA, are indeed enabled by the instant specification. The experiments described in Examples 2 and 4 with B7-H1-specific antibodies in the sera of RA patients (Example 2) and B7-H1-specific monoclonal antibodies (Example 4) cumulatively indicate that pathology-mediating T cells are activated, at least in part, by a process involving costimulation of the T cells by B7-H1-specific antibodies in the patients. As stated on page 1, lines 16-18, of the instant specification and on page 370 (column 1, penultimate sentence of the second full paragraph) of the Dong et al. reference cited by the Examiner, elevations in B7-H1-specific antibodies similar to those described in detail in RA patients were also seen in systemic lupus erythematosus (SLE) and autoimmune hearing loss (referred to as "autoimmune inner ear disease" in Dong et al.) patients, the three diseases having extremely diverse symptoms and target organs/tissues. In light of these teachings, one skilled in the art would expect that, in at least a subset of patients with any of a wide range of conditions in which symptoms are caused directly or indirectly by activated T cells (see the entire specification), elevated levels B7-H1-specific antibodies would very likely be found. Such an artisan would thus also expect that the claimed methods would be useful in the diagnosis and disease stage monitoring of such conditions.

With respect to the comments on page 9, lines 10-16, of the Office Action, Applicants respectfully submit that the above comments with respect to there being no requirement that any given method or process perform with 100% efficiency for patentability are apropos to the Examiner's remarks on the Merrill et al. reference. Moreover, the statement in Merril et al. immediately following that quoted by the Examiner indicates that several of the biomarkers referred to by the authors are in fact useful as "indicators of flare and remission" in SLE (page 712, paragraph 2).

Thus, in light of the above considerations, Applicants respectfully submit that the working examples, the teaching and guidance of other parts of the specification, and the general knowledge of those skilled in the art enable performance the methods of the instant claims by such artisans without extensive and undue experimentation. Therefore, Applicants request withdrawal of the rejection under 35 U.S.C. § 112, first paragraph.

CONCLUSION

In summary, in view of the amendments and remarks set forth above, Applicants maintain that all of the pending claims now patentably define the invention. Applicants request that the Examiner permit the pending claims to pass to allowance.

If the Examiner would like to discuss any of the issues raised in the Office Action, Applicants' undersigned representative can be reached at the telephone number below.

Enclosed are a request for an automatic extension of time and check in payment of the extension in time. Please apply any charges or credits to Deposit Account No. 06-1050, referencing Attorney Docket No. 07039-443001.

Respectfully submitted,

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